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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/083,793	05/22/98	MURPHY B	17634-000320

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EXAMINER	
MOSHER, M	
ART UNIT	**PAPER NUMBER**
1643	10

DATE MAILED: 12/17/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/083,793	Murphy et al
Examiner	**Group Art Unit**
Mosher	1641

☒ Responsive to communication(s) filed on *7/10/98, 1/22/99, 1/28/99, 9/27/99*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-143* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-143* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *10*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1641, Examiner Mosher.

Election/Restriction

After search of the elected species, it was determined that search of the full scope of the invention would not be unduly burdensome, despite the large number of claims and species recited in the claims. Therefore the requirement for election of species is withdrawn.

Since there is no provision for "contingent" amendments, the amendment filed 9/27/99 has been entered. Applicant has the option of further amending the claims to restore the original subject matter, if desired.

Claim Objections

Claims 6-9, 17, 55, and 68 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 6-9 appear to expand rather than limit the parent claim, because RSV and measles are not "heterologous PIV sequence" as required by the parent claim. Claim 55 appears to expand rather than limit the parent claim, since "coinfection with PIV" is not normally considered as "an expression vector" as required by the parent claim. Claim 17 appears to expand rather than limit the scope of claim 15, in reciting "at a position

corresponding to .... of JS cp45", while parent claim requires "one or more attenuating mutations *of* JS cp45". A mutation at a corresponding position encompasses mutations different from the specific mutation of the parent strain, since different mutations can be made at the same position. Claims 68 has the same problem.

Claim Rejections - 35 USC § 112

Claims 15, 16, 19, 30, 36, 37, 39, 65-69, 71, 72, 78, 81, 82, 105, 106, 109-111, 113, 114, 127, 128, 130-136, 138-141, and 143 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 110 are confusing in depending from higher-numbered claims.

Claims 132, 134, 136, 140, 141, and 143 are confusing in requiring "a full complement" of mutations present in JS cp45, and in stating that the "full complement" comprises a list of specific mutations. Is the intent to require all of the specific mutations, or to require ***all*** of the mutations present in JS cp45, including those not recited in the list? Furthermore, in claims 39, 111, 131, 139, it is not clear how the virus can have "up to the full complement" of JS cp45 mutations, and still meet the requirements of the parent claims regarding replacement of the starting PIV genome with genes from other species of PIV. Since the mutations of JS cp45 apparently occur in all of the virus genes and the 3' untranslated regions, how can any of the genes be replaced without removing part of the "full complement" of cp45 mutations?

Also, claims 132, 134, 136, 140, 141, and 143 as amended are confusing, in reciting "i)...ii)...iii)...v)...vi)..." without including "iv".

Still further, are claims such as 37, 69, 72, 82, and 114 correct in reciting that JS cp45 has attenuating mutations in the N protein sequence and the leader sequence? This contradicts the prior publication by Stokes et al, see Figure 2. In applicant's specification, page 92 suggests that mutations in JS cp45 were not fully described in the prior art; if that is the case, the metes and bounds of "mutations in JS cp45 " are not clear, rendering claims 15, 30, 36, 37, 39, 65, 69, 71, 78, 81, 82, 105, 109-111, 113, 114, 127, 128, 130-132, 134, 136, 138-141, 143, and dependent claims 16, 66-68, 67, 106, 133, and 135 unclear. If "JS cp45" does not have the structure described in the publication by Stokes et al (Virus Research 30:43-52, 1993), then deposit of "JS cp45" will be required to enable claims that require access to materials obtained from "JS cp45" for a reproducible method of making the claimed materials.

Claims 15, 16, 30, 31, 36, 37, 39, 65- 69, 71, 72, 78, 81, 82, 105, 106, 109-111, 113, 114,117, 127, 128, 130-136, 138-141, and 143 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As discussed above, after reading applicant's specification, it is not clear if "JS cp45" has the same structure as the publicly available material described in the publication by Stokes. It is apparent that JS cp45 is required to practice the claimed invention, for claims that specifically require part of the "JS cp45" genome. As a required element it must be

known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the "JS cp45" strain used as starting material in the specification. The specification does not provide a repeatable method for obtaining "JS CP45" and it does not appear to be readily available material, if the structure differs from the publicly available material.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 102

Claim Rejections - 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 7, 10-17, 20, 21, 26, 27, 30, 33-40, 43, 44, 47-49, 52, 54, 56, 57, 59, 61-85, 88-91, 93, 94, 96-116, 118, 120-143 are rejected under 35 U.S.C. 102(e) as clearly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Belshe et al (5,869,036). See the patent claims, and column 9, line 66, through column 10, line 41. Although Belshe et al does not provide a working example of the material set forth in applicant's claims, Belshe et al contains sufficient disclosure to enable hybrid viruses produced by use of nucleic

acids such as those claimed by applicant, and to enable hybrid viruses and their method of production. See patent claims 1-42, which are legally presumed to be enabled by the corresponding disclosure. For the materials claimed in the patent claims, the patent anticipates the invention as claimed; for those materials that differ from precisely what is claimed in the patent (e.g., isolated polynucleotides), the patent explicitly suggests those materials. Therefore, the invention as a whole is anticipated, or rendered prima facie obvious, over the patent claims and the supporting disclosure.

Claims 5, 8, 9, 45, 46, 51, 53, 86, and 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belshe et al. Claims 5, 8, 9, 45, 46, 86, and 87 differ from the subject matter of the patent claims in that they require the presence of a heterologous sequence from bovine parainfluenza virus or measles virus. At column 8, line 27- column 9, line 5, and in Example 7, the patent explicitly suggests such a chimeric virus. It would have been within the ordinary skill of the art to carry out the explicit suggestion, with reasonable expectation of success. Claims 51 and 53 differ from the patent claims in requiring PIV genome and the N, P, and L proteins to be expressed from a single vector instead of plural vectors. However, it would have been within the ordinary skill of the art to modify the teachings of Belshe et al to include all of the required nucleic acid sequences in a single vector, for the purposes of convenience in reducing the number of transformation events required for production of virus. Therefore, the invention as a whole is seen as prima facie obvious, absent unexpected results.

Claims 18, 19, 28, and 29 are rejected under 35 U.S.C. 102(e) as anticipated by Belshe et al, or, in the alternative, under 35 U.S.C. 103(a) as obvious over Belshe et al in view of Stokes et al (Virus Research 30:43-52, 1993). These claims specify particular substitutions in the N protein region. If applicant's specification is correct in stating that these mutations are present in the JS cp45 genome, then Belshe et al inherently anticipates these claims, because Belshe et al requires the N protein region from cp45 in some of the patent claims. Alternatively, if these mutations are not inherently present in cp45, Stokes et al teaches these changes in another attenuated vaccine strain of hPIV3, and it would have been within the ordinary skill of the art to introduce such attenuating mutations into the claimed chimeric virus genome, for the purpose of further attenuating the chimeric virus. Therefore, if not inherently anticipated by the patent claims, the invention as a whole is seen as prima facie obvious, absent unexpected results.

Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Belshe et al as applied to claims 5, 8, 9, 45, 46, 86, and 87 above, and further in view of Karron et al (Journal of Infections Diseases 171:1107-14, 1995). This claim differs from above in requiring the heterologous sequence in a chimeric PIV to contain a mutation affecting any of a group of phenotypes. Karron et al teaches an attenuated bovine PIV useful in human vaccination; it would have been obvious to use genes from an attenuated BPIV in the chimeric PIV suggested by Belshe et al, to avoid increasing the virulence of the chimeric virus by introduction of wild-type genes in the chimeric virus. Therefore the invention as a whole is seen as prima facie obvious, absent unexpected results.

Claims 22-25, 31, 32, 42, 60, 117, and 119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belshe et al in view of Conzelmann (Journal of General Virology 77:381-389, 1996). These claims differ from the claims of Belshe et al, in that they do not require a chimeric PIV containing heterologous F or HN genes, but instead require incorporation of mutations from the F or HN genes of cp45, or require production of wild-type PIV, or require use of a cis-acting region from a different species of PIV, or require use of a 'subviral particles" in an immunogenic composition. Conzelmann reviews progress and perspectives in genetic engineering of other negative-stranded RNA viruses. Conzelmann discusses recombinant production of genetically-marked wildtype viruses, manipulation of cis-acting sequences and each viral protein in engineered viruses, and use of defective viruses. Considering that each of these variations is discussed or suggested by the review for analogous viruses, one of ordinary skill in the art would have been motivated to modify the teaching of Belshe et al to produce viruses such as those discussed in the review. Therefore the invention as a whole is seen as prima facie obvious, absent unexpected results.

Claims 11, 48, 50, 52, 55, 56, 58, 91, and 92 are rejected under 35 U.S.C. 102(b) as being anticipated by Dimock et al (Journal of Virology 67:2772-2778, 1993). Claim 52 is drawn to a method for producing an infectious PIV particle. Dependent claim 55 indicates that the "expression vector" of claim 52 encompasses PIV itself. Claim 58 requires a "subviral particle", and thus indicates that "PIV" is meant to encompass "subviral particles". Specification page 6 defines "subviral particle" sufficiently broadly to encompass any defective PIV. Therefore, the

invention, as claimed, reads upon the method of producing defective PIV taught in Dimock et al, and upon the polynucleotides used int the method and the infectious defective particles produced.

Claims 11, 48, 49, 52, 54, 57-59, 60, 91, and 93 are rejected under 35 U.S.C. 102(a) as being anticipated by Kato et al (Genes to Cells 1:569-579, June 1996). Kato et al teaches a murine PIV (Sendai virus) polynucleotide, methods, and recombinant virus meeting each and every claim limitation.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 16, 1999

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600